other genetic diseases described by Rimoin, which are associated with diabetes, support the heterodisperse nature of the inherited defect, and, from a biochemical basis, demonstrate that any number of mutations resulting in a broad array of other inherited abnormalities may be associated with diabetes. This again suggests the Beta cell is more "fragile" or limited as far as its regenerative capacity is concerned.

One may ask why the Beta cell has been selected out as the weak link—why not the thyroid cell, or that in the adrenal cortex? The hair follicles in many males and some females and the ovarian cortex in all females also undergo an earlier senescence, but these are relatively dispensable tissues as compared with the Beta cell. The riddle cannot be answered as yet, unless mild diabetes might have offered at one time some degree of selective advantage.[7]

Finally, is the entire constellation, mentioned in the first sentence of this editorial, simply a result of the Beta cell deficiency? Many investigators feel it is, and there are recently published biochemical data in support,[8] but until long-term insulin and carbohydrate homeostasis is maintained by an artificial pancreas, or by successful long-term transplantation of Beta cells or even by rejuvenation of Beta cells remaining in the diabetic (all these possibilities are now being put to experimental test[9]), one cannot answer with confidence. The vast majority of those in the field, however, act as if the complications result from the disturbed insulin-carbohydrate homeostasis, and treat the disease accordingly.

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Some Caveats for the FDA

RECENT DECISIONS by the United States Supreme Court appear to give the Food and Drug Administration (FDA) very significant powers to decide what drugs and medicines can be marketed in the United States. A federal bureau will now have real power to decide which drugs a physician may prescribe for what purpose in caring for his patients, and those which he may not. This is a very considerable power which strikes very close to home for physicians and patients alike. And unless it is exercised wisely and with an understanding of human nature and human needs and the realities of clinical medicine, it may not be very popular.

The Supreme Court opinion itself, written by Associate Justice William O. Douglas, traces the growth of FDA authority and responsibility since 1906. The 1906 Food and Drug Act provided for criminal sanctions and seizure for condemnation of drugs found to be *adulterated* or *misbranded.* The Food, Drug and Cosmetic Act of 1938 established a system of pre-marketing clearance for drugs, the emphasis being upon the *safety* of the drug. The 1962 amendment of the 1938 Act directed the FDA to refuse approval of a new drug application if "substantial evidence" that the drug is *effective* for its intended use is lacking. The 1973 decisions of the Court now give the FDA the power to force drugs it deems to be ineffective off the market, to issue strict rules governing product effectiveness, to deny hearings to manufacturers on contested actions, and to proceed against entire product classes rather than individual drugs. These are significant and substantial powers.

While the distinction between a drug that is adulterated or misbranded and one that is not is clear enough, this clarity of distinction blurs somewhat when it comes to deciding upon safety and effectiveness. There are very few drugs that are entirely safe and always effective. There is nearly always some element of danger in the administration of any drug. Safety is therefore a matter of degree, and the degree is often a matter of conjecture since it depends upon effects of the drug which may not be known and upon the reaction or response of an individual patient which is never entirely predictable; and it is paradoxically true that

the scientific proof of the effectiveness of a given drug usually follows rather than precedes clinical experience with it, and this proof may take years to establish. In practice, both the safety and effectiveness of a drug in a given circumstance are apt to be considered in terms of probabilities. The size of the risk to be taken in terms of safety and probable effectiveness is a matter to be decided by the physician with the informed consent of the patient. In serious or desperate situations, quite sizable risks may be opted by physicians and patients alike, and if these options should become too restricted by bureaucratically imposed criteria of safety and effectiveness for the intended use, some patients who are most in need may be deprived of the chance of relief or cure which should be their right. It is suggested that judgment, a judgment that is in many ways related and similar to clinical judgment, should be exercised by the FDA in determining what risks are acceptable in the marketing of drugs.

Human nature and human needs will affect both the actions taken by the FDA and the response to these actions on the part of physicians, patients and the public; and it is possible that the restraints imposed by the Supreme Court on the use of court actions to stay or reverse any FDA decisions may intensify some of these responses as time goes by. A few caveats are offered:

- There will be an understandable and very human temptation for the FDA bureaucracy, in order to protect itself, to err in the direction of prohibiting the marketing of a drug if there is any chance that it may be unsafe or ineffective. Not only can this deprive Americans of drugs which can be used with benefit, and are being so used elsewhere in this world, it can be a serious deterrent to progress in drug development in this nation. This of course would be a disservice to the public which is to be served.

- Human nature is such that many persons believe in drugs and rely upon them for relief of real or fancied ailments. There is some evidence that Americans are particularly drug-oriented in this sense. It is suggested that a case can be made for permitting the sale of some relatively harmless and relatively ineffective drugs to satisfy these human needs.

- Simply ordering a drug off the market does not assure its disappearance. Experience has shown that if there is a human need or a strong desire for a drug, the American people are capable of developing alternative means of supply which can make mockery of both the law and its enforcement.

It is clear that much will depend upon the wisdom and statesmanship with which the new FDA powers are used. The aim, to rid the market of unsafe and ineffective drugs, is laudable and to be supported. We suggest that success will not come easily for many reasons, some of which have been given here. We suggest that success will be more likely if clinical realities and human needs and human nature are all taken into account when the decisions are made. And we further suggest that the FDA involve all those who should be involved—that is, practicing physicians, consumers, and, of course, the pharmaceutical industry—in its decision-making processes.

—MSMW

A Case for "Backlash"

IN HIS ARTICLE "Backlash—The Case for American Medicine," which appears elsewhere in this issue, Francis D. Moore borrows part of his title from Schwartz's well known book,[1] and then proceeds to carry the case for American medicine considerably further. In his address to the graduating class of one of California's medical schools, Dr. Moore forthrightly considers the gamut of recent attacks on American medicine and some of the reasons for them, and provides much valuable information and formidable logic for what he suggests is an overdue rejoinder from American medicine against these attacks. In particular he deplores political polarization where medicine and health care are concerned and emphasizes that usually there are worthwhile values in both the opposing views. He points out that as scientists we learn to see both sides of problems and urges us as physician politicians to persuade others to see likewise.

There is much of positive thought in Dr. Moore's article and it is well worth careful perusal by all physicians, and especially by those who feel that the time has come for more of a rebuttal against the recent and current rash of attacks on American medicine. Dr. Moore presents a considerable amount of ammunition for such a rebuttal.

—MSMW

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